Dissertation on

PRIMARY LUNG CANCER IN FEMALES – A DESCRIPTIVE STUDY

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Institute of Thoracic Medicine
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CERTIFICATE

This is to certify that the dissertation **"PRIMARY LUNG CANCER IN FEMALES – A DESCRIPTIVE STUDY"** is the bonafide original work of Dr.D. Nancy Glory in partial fulfillment for M.D.BRANCH-XVII (T.B. AND RESPIRATORY DISEASES) EXAMINATION of the Tamilnadu Dr. M.G.R. University to be held in March 2008. The period of study was from June 2006 to August 2007.

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DECLARATION

I, **Dr.D. Nancy Glory**, declare that dissertation titled **"PRIMARY LUNG CANCER IN FEMALES – A DESCRIPTIVE STUDY"** is a bonafide work done by me at Institute of Thoracic Medicine, Chetpet and Department of Thoracic Medicine, madras Medical College & Govt. General Hospital, Chennai-3 under the guidance of my Professor **Dr.D.Ranganathan, M.D. DTCD Dip.N.B.**

This Dissertation is submitted to the Tamilnadu Dr.M.G.R.Medical University towards partial fulfillment of requirement for the award of **M.D.Degree Branch-XVII (T.B. AND RESPIRATORY DISEASES)**.

Place: Chennai

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CONTENTS

INTRODUCTION

Lung cancer is a major health problem worldwide. The incidence is increasing globally at a rate of 0.5% per year. It is the leading cause of cancer mortality in most of the countries in the world. It remains the most lethal form of cancer in men and has now surpassed breast cancer in women as well in USA, where 170,000 new cases are diagnosed per year. But in India Lung cancer is second only to breast cancer in females. The worldwide incidence is 14% whereas it constitutes 6.8% of all carcinomas in India. The increase whether due to the actual increase or due to the improvement in diagnostic techniques needs to be clarified? Complex circumstances like genetic predisposition, environmental exposure, life style habits combine over a lifetime to initiate and promote tumor growth in the lung. Despite advances in imaging techniques and treatment modalities, the prognosis of lung cancer remains poor, with a five-year survival of 14% in early stages and less than 5% in locally advanced stages. Unfortunately only 20-30% of patients present with an operable disease, while most of the patients present in an advanced stage III and IV. The main reason for late presentation in our country is the poor health awareness, delayed recognition and the poor referral of patients to the specialized centers

AIM OF THE STUDY

To study the Clinicopathological, Radiological profile, possible associated risk factors and diagnostic modalities of Primary Lung Cancer in females.

DESIGN OF THE STUDY

Prospective

This study was examined and approved by the Ethical Committee of the Institution.

REVIEW OF LITERATURE

Lung cancer is the major cause of cancer-related death in both men and women. Emerging evidence indicates that there are differences in the pathogenesis and possibly increased susceptibility to lung cancer in women. In addition, considerable data support small, but important differences favoring women in terms of response to therapy and long-term survival after the diagnosis of lung cancer, regardless of histology or stage. These differences in both biology and outcome will be important considerations in the design of future trials of screening and therapy for lung cancer.

There has been a fourfold increase in lung cancer in women over the past 30 years and it is estimated that this rise will not plateau until after 2010. This increase in lung cancer in women has been referred to as a **contemporary Epidemic**. The rise in lung cancer-related mortality among women has significantly altered the male/female ratio in this disease

While much of this altered epidemiology can be attributed to changing patterns of tobacco use, it is becoming increasingly apparent that the relative risks (RRs) of specific types of lung cancer, the relationship between smoking and lung cancer, as well as the response to therapy may not be the same for both sexes. There are several differences between lung cancer in men and women that are of growing importance and may impact on diagnosis, treatment, and outcome.

Sex Differences in Lung Cancer

Characteristics	Sex Differences
Risk	Women may be at greater risk for lung cancer than men
Molecular variables	Different metabolism of tobacco-related carcinogens Possible association with HPV infection Women have relatively less DRC
Response to therapy	Women have increased response rates to cisplatin-based chemotherapy compared with men
Outcome	Women have better outcome stage for stage than men

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Risk Factors

Smoking

Smoking is the overwhelming cause for lung cancer in both men and women; 85 to 90% of patients with lung cancer are current or former tobacco smokers. Smokers are 22 times more likely to die from lung cancer than nonsmokers (41). Although smoking is a risk factor for all histologic types of lung cancer, the association is stronger for small cell, squamous cell, and large cell carcinoma than for Adeno Carcinoma. Death rate from smoking-related disease for men has leveled off, women's rates continue to rise, both as a delayed effect of past smoking and a lower rate of smoking cessation.

Environmental Tobacco Smoke

Environmental tobacco smoke (ETS) accounts for approximately 3,000 lung cancer deaths each year in the United States among nonsmokers, primarily women. A nonsmoking woman has a 24% greater risk of lung cancer if she lives with a smoker (41). Urinary levels of nicotine, cotinine, 4-(methylnitrosamino)- 1-(3-pyridyl)-butanol (NNK), a tobaccospecific carcinogen, and its glucuronide (NNALGluc) were elevated in nonsmoking women exposed to ETS compared to those who were not exposed.

Indoor Air Pollution

Domestic cooking is an important duty of an average Indian housewife. On an average, an Indian woman spends about four to six hours daily for cooking. Mainly four different types of cooking fuels are used in this country. Biomass fuel (Wood, Cow-dung cake, agricultural waste, coal etc.), liquefied petroleum gas (LPG), kerosene and a mixture of these. About 95% of the rural population in India still relies primarily on biomass fuels (dung, crop residues, and wood). Use of these fuels causes a number of respiratory problems, which include acute respiratory infections in children, chronic obstructive lung disease in non-smokers. It has also been implicated as a risk factor for lung cancer in women (12). Biomass smoke, however, contains a wide-range of chemicals that are known or suspected human carcinogens. Thus, they may be important risk factors for development of Lung Cancer. Coal smoke contains many potential carcinogens

like SO_2, CO, Radon and thoron. Use of Kerosene for cooking has also been seen associated with development of Lung Cancer as reported in some studies.

Radiation

Exposure to radiation may be from an external source (such as a therapeutic X-ray apparatus or a nuclear bomb) or by inhalation of radioactive gases. Radioactive gas is related primarily to radon a substance formed during the decay of Uranium to stable lead. Occupational exposure to radon and its progeny occurs in workers involved in mining Uranium, fluorspar, niobium and other substances or in the processing of radioactive materials.

Patients who have Hodgkin's disease or breast carcinoma and who have been treated with supra diaphragmatic radiation or combined modality therapy also may have a slightly increased risk for the development of pulmonary carcinoma.

Family History

Patients with lung cancer have a higher number of relatives with lung cancer than control subjects. The simplest explanation of this phenomenon is the clustering of cigarette smokers within families. While undoubtedly true, there is also an increased risk of lung cancer regardless of family smoking history. This finding suggests that genetic and perhaps other shared environmental factors may be present in this population.This risk was found to be greater for

adenocarcinoma of the lung. , the risk was found to be greater in women than in men, and again adenocarcinoma was the predominant tissue type.

Occupational Risk for Lung Cancer

Certain occupations carry a higher risk of lung cancer. The following occupational exposures are known to be associated with an increased risk: (a) Asbestos: insulation workers and shipyard workers are exposed to asbestos. There is some increase in the risk of lung cancer after 10 years of exposure and a substantial risk after 20 years of exposure. Concurrent smoking increases the risk to 90 fold; (b) Arsenic: smelter workers and vineyard workers are exposed to arsenic. The risk is dose related. Lung cancers have an upper lobe predominance and there may be multiple primaries; (c) Nickel refinery workers : squamous cell carcinoma is more common; (d) Radiation (Uranium mining): oat cell carcinoma is more common; (e) Haematite mining: due to radon exposure; (f) Hard rock mining; (g) Chromium exposure in ore mining and pigment manufacturing: squamous cell variety is most common; (h) Chloromethyl exposure in workers in industries: oat cell carcinoma is most common; (i) Ethers and mustard gas: squamous and undifferentiated carcinomas are most common; (j) Soot, tars exposure in coke oven workers and (k) Oils and coke exposure in Gas house workers, roofers and rubber workers. Other occupational exposures that are suspected include those to acrylonitrite, berrylium, and dimethyl sulphate. No systematic information on occupational risk for lung cancer patients is available in India.

DIET AND LUNG CANCER

There is some evidence that certain dietary factors may be protective for lung cancer, and others may increase the risk. There are conflicting reports about the role of betacarotene and lung cancer, although most reports suggest a protective effect. Case control studies from China have shown that vegetable intake is a protective factor for lung cancer. Pumpkins and onions had the most consistent protective effect. On the other hand, animal food products and dairy products have a predisposing effect on lung cancer. Dietary cholesterol and animal fat increases the risk of lung cancer. Behera et al (13), however, reported that b-carotene and vitamin A levels and vitamin C levels in patients with lung cancer compared to healthy controls were not significantly different.

Patho biology

The development of lung cancer is the end result of a complex interplay of factors including carcinogen exposure, metabolism, and genetics. Tobacco smoke, recognized to be the foremost risk factor for lung cancer, contains more than a hundred diverse mutagens and carcinogens, including polycyclic aromatic Hydrocarbons, N-nitro amines, and aromatic amines. The initiating activity remains for an extended period after the cessation of smoking.

Two classes of enzymes play a crucial role in the metabolism of tobacco-related carcinogens: the phase I and II detoxifying enzymes. While phase I

enzymes (*ie*, cytochrome P450, monooxygenases) activate carcinogens to reactive intermediates, their action is balanced by phase II enzymes, which serve to convert these same reactive intermediates (*ie*, reactive oxygen species) to inactive conjugates that are more water soluble and hence excreted more readily. Polymorphisms have been found to alter the metabolic activity of detoxification enzymes. Those active metabolites that are not detoxified bind to DNA forming DNA adducts. Women have higher levels of these DNA adducts when compared to men.

Many genetic and epigenetic alterations of tumor suppressor genes have been demonstrated in lung cancer. The most frequent genetic alterations found are in p53 (in 90 % of small cell lung cancers [SCLCs] 40 to 70% of non-small cell lung cancers [NSCLCs]) and in oncogenes such as K-ras. The p53 pathway has long been recognized as playing a key role in cell cycle regulation by causing arrest in both the G1 and G2 phases in cell division in response to DNA damage. This arrest allows for DNA repair or apoptosis. P53 mutation leads to abrogation of this arrest and perpetuation of DNA damage and consequent inhibition of the normal apoptotic mechanism. Smoking has been found to induce p53 mutation via the formation of DNA adducts. Women have been found to have higher levels of pulmonary DNA adducts per pack-year than men Of the Ras family of proto-oncogenes, K-ras is the most frequently affected gene. As in the p53 genemutation, the formation of DNA adducts secondary to the effects of smoking appears to play a pivotal role. Women are three times more likely to carry the K-

ras mutation than men. In most studies, Ras mutations are predominantly associated with adenocarcinoma.

Growth Factor Receptors

Certain growth factors have been shown to stimulate the growth of both normal and neoplastic cells in the lung. A receptor for the autocrine growth factor, gastrin releasing peptide receptor (GRPR), has been identified in both small cell lung cancer and NSCLC. The GRPR gene is on the X chromosome and escapes X-inactivation. It is expressed more frequently in female nonsmokers (than male) and is activated earlier in response to tobacco exposure.

ERBB2 (HER-2/neu) is one of four receptor-type tyrosine kinases that form a heterodimer with other members of the ERB-B class and mediates cell growth and survival. Previously, several surgical series found that over expression of HER-2/neu is associated with a poorer prognosis and survival. HER-2/neu is most commonly expressed in Adeno carcinoma, the most common subtype in women.

DNA Repair Capacity

An emerging literature implicates differences in DNA repair capacity (DRC) in both the pathogenesis of lung cancer and response to therapy. A complex Family of proteins exist to remove damaged DNA segments or to repair mismatched nucleotides. Deficiencies in this process are unequivocally mutagenic and carcinogenic.

Paradoxically, this relative deficiency in DRC may relate to the observation that women have better responses and survival when treated with platinum based chemotherapy.

Hormonal Influences

The most obvious biological differences between the male and female are hormonal. An estrogen driven environment is a recognized factor in the Pathogenesis of breast, endometrial, and ovarian cancers. With the increasing rates of lung cancer in women and their increased susceptibility to the detrimental effects of tobacco smoke compared to men, the role of female steroid sex hormones has been hypothesized to be a factor in lung carcinogenesis. Estrogen receptors are abundantly expressed in normal lung tissue and in lung tumor cell lines at the messenger RNA level. Estradiol has a proliferative effect on normal lung fibroblasts and lung cancer cell lines *in vitro*. There was a 17-fold increase in cellular proliferation in lung cancer-derived cell line as opposed to only a 3.8-fold increase when normal lung fibroblasts were incubated with _-estradiol. This finding suggests an increased responsiveness of malignant clones to estrogen. The exact role of estrogens in lung cancer is not clear, but they may act as direct carcinogens via the formation of DNA adducts. early menopause was associated with a decreased risk of Adeno carcinoma in women. Soy phytoestrogens have been shown to compete with endogenous estradiol for ERs and have been shown to have a protective effect against lung cancer. Premenopausal women tended to present with more extensive disease and

Adeno carcinoma than postmenopausal women. Favorable prognostic factors: low-stage disease, surgical therapy, age _ 50 years, and female sex.

1999 WHO Histological Classification of Lung Tumors

A. Squamous cell carcinoma (epidermoid carcinoma)

Variant:

- Papillary
- Clear cell
- Small cell
- Basaloid

B. Small-cell carcinoma

Variant:

- Combined Small cell carcinoma

C. Adenocarcinoma

- Acinar
- Papillary
- Bronchio-alveolar carcinoma
- Solid carcinoma with mucin
- Adenocarcinoma with mixed sub types

Variants:

- Well differentiated fetal Adenocarcinoma
- Mucinous (Colloid) Adenocarcinoma
- Mucinous cystadenocarcinoma
- Signet-ring Adenocarcinoma
- Clear cell adenocarcinoma

D. Large-cell carcinoma

Variants:

- Large Cell neuroendocrine Carcinoma
- Basaloid Carcinoma
- Lymphoepithelioma like Carcinoma
- Clear cell Carcinoma
- Large cell Carcinoma with rhabdoid phenotype

E. Adeno Squamous carcinoma

F. Carcinomas with pleomorphic, sarcomatoid or sarcomatous elements

- Carcinomas with spindle and/or giant Cells
- Pleomorphic Carcinoma
- Spindle Cell Carcinoma
- Giant Cell Carcinoma
- Carcinosarcoma

· Blastoma (pulmonary blastoma)

· Others.

G. Carcinoid Tumor

· Typical Carcinoid

· Atypical Carcinoid

H. Carcinomas of Salivary Gland type

· Adenoid cystic carcinoma

· Mucoepidermoid carcinoma

I. Unclassified Carcinoma

The selection of therapy is becoming more specifically related to tumor histology. The histopathologic appearance of lung carcinoma remains an important guide to prognosis and treatment.

Clinical Manifestations

Lung Cancer presents with diverse clinical manifestations. Clinical features may be due to the following reasons.

Clinical features due to primary tumor

Centrally located tumors produce different symptoms than do peripherally located tumors.

Clinical features due to central tumors

Cough

It is the commonest symptom and occurs in 75 % or more of patients. Cough may be produced by a small tumor acting as a foreign body interfering with bronchial peristalsis or by neoplastic erosion of bronchial mucosa.

Hemoptysis

It occurs in 5 to 51 % of patients. It is usually scanty and is due to ulceration of bronchial mucosa.

Chest pain

It is vague, persistent and poorly localized. It is due to peribronchial and perivascular nerve involvement.

Dyspnoea

It occurs in approximately 58 % of patients. It may be due to emphysema, pleural effusion, atelectasis, bronchopulomonary infection, phrenic nerve paralysis and O_2 transport defect in bronchioloalveolar carcinoma.

Wheeze

It occurs in 2 % cases. It is due to fixed mechanical obstruction below the carina & it is not changed after cough.

Stridor

It is due to narrowing of trachea and main bronchi at about the level of carina.

Fever and sepsis

It is due to post obstructive pneumonia.

Clinical features due to peripheral tumors

Pleuritic Chest Pain

It is either due to involvement of the parietal pleura or due to pleurisy arising as a result of post obstructive segmental or subsegmental pneumonia.

Dyspnoea

It is restrictive in nature. It is either due to pleural effusion or due to pleuritic chest pain.

Cough

It is less common except in brochioloalveolar carcinoma.

Clinical features due to intrathoracic spread

Neurological complications

Due to involvement of 8^{th} cervical and 1^{st} thoracic nerve the patient will present with characteristic pain in the shoulder and in the arm along the distribution of ulnar nerve. Sensory loss with weakness and wasting of small muscles of the hand will occur. Patient may present with horner syndrome due to involvement of cervical sympathetic nerve. Involvement of recurrent laryngeal nerve produces hoarseness of voice & dysphagia (common on the left side). Diaphragmatic palsy due to phrenic nerve damage is a possibility. Erosion of the ribs (commonly 1^{st} and 2^{nd}) may occur.

S.V.C Obstruction

It is obstructed either by primary tumors or by metastatic lymph nodes. It was first described by William Hunter in 1757. Obstruction may be above or below the azygos vein. The most common presenting symptoms are oedema of the head, neck, arms and breast, dyspnoea, cough and orthopnoea. The oedema

is pitting and varies with changes in position. Collateral veins fill from above downwards. Its incidence ranges from 4 to 19 %.

Pleural and pericardial effusion

Pleural effusion is commonly due to direct involvement of pleura by tumor. It may be due to lymphatic obstruction or disruption of thoracic duct (chylothorax). Features of cardiac tamponade, sinus tachycardia or atrial fibrillation may appear due to involvement of pericardium or heart.

Dysphagia

It may occur due to compression of oesophagus by posterior mediastinal node. Immediate cough upon swallowing may occur due to broncho-pleural fistula.

Pulmonary artery constriction or pulmonary artery stenosis (extrinsic) may occur due to tumor involvement.

Clinical features due to extrathoracic metastasis

Extrathoracic metastasis is common in small cell carcinoma. It may involve any organ or tissue, but lymphnode, bone, brain, liver, adrenals and skin are commonly involved. Bone and Brain involvement usually produces symptoms and others are usually silent.

Central Nervous system

Metastasis may involve the brain, meninges and spinal cord. Spinal cord involvement produces back pain which is localized and progressive in nature. Other symptoms are numbness, tingling, weakness of an extremity, bladder and bowel disturbance and unsteadiness of gait. Due to intracranial involvement patient may present with headache, vomiting, altered mental status, weakness, seizures, cranial nerve abnormality, hemiparesis and cerebellar ataxia.

Lymph node metastasis

Lymphatic spread is more common in small cell carcinoma. The whole of right lung and lower lobe of left lung ultimately drains in to right supraclavicular node via hilar and paratracheal nodes. Upper lobe of left lung drains in to the para aortic, hilar and carinal nodes. Enlarged node is usually painful and hard in consistency.

Bone metastasis

It produces distressing and unremitting pain which may be due to pathological fracture or bone erosion.

Hepatic metastasis

Enlarged palpable liver and jaundice are unusual. Hard and irregular liver suggest hepatic metastasis.

Skin metastasis

It may occur occasionally.

Paraneoplastic Syndrome

Paraneoplastic syndromes are non-metastatic metabolic or neuromuscular complications of lung cancer. It occurs most commonly in small cell carcinoma. Ectopic hormones are produced from the neurosecretory granules within the malignant cells.

a. Metabolic Disorders

Hypercalcemia

It is caused by ectopic parathormone secretion by tumor cells. It commonly occurs in squamous cell carcinoma. It is seen in about 10 % of cancer patients. Patients present with thirst, polyurea nocturia, nausea, vomiting, anorexia, abdominal pain, mental confusion, hypotonia, stupor and ultimately coma.

Syndrome of inappropriate antiduresis

It is commonest of the syndromes of tumor hormonogenesis (2-22 %) and common in small cell carcinoma. Patients present with headache, drowsiness, mental confusion, disorientation, convulsion, coma, hypothermia and death.

Clinical syndrome due to excess ACTH

It is fairly uncommong (< 2 %) and is widely variable in severity. Patients present with dependent oedema, pigmentation, weakness and wasting of muscles particularly of limb girdle. Hypertension and hyperglycemia may be present. Cushing's syndrome is unusual.

Clinical syndrome due to other hormones

Oxytocin, GHRH, somatostatin, neurophysin, liptrophin, prolactin, calcitonin gastrin, glucagons etc may be produced by tumor cells. Very rarely these hormones produce symptoms.

b. Neurologic and Neuromascular disorders

Peripheral neuropathy

Commonly seen in small cell carcinoma. It may be motor, sensory or mixed and may be accompanied by muscle wasting or weakness.

Autonomic neuropathy

It may produce postural hypotension and disturbance of intestinal motility. Cerebellar ataxia with nystagmus, impaired co-ordination and dysarthria may occur.

Polymyositis/dermatomyositis syndrome

It is characterized by proximal muscle weakness, pain and tenderness and a characteristic facial heliotrope rash.

Myasthenic syndrome

Patients present with muscle weakness and in contrast to myasthenia gravis it improves with repeated effort. Other differentiating points are muscular wasting, loss of tendon reflex and infrequency of bulbar involvement.

Hypertrophic Pulmonary Osteoarthropathy

It was first described by Bomberger (1889) and Marie (1890). Thompson (1904) first described its associated with lung cancer. Its incidence varies from 2 to 48 %. Patients present with bone pain in the involved areas which are often hot and tender to touch. There may be associated pain and swelling of wrists, ankles and knee joints. Clubbing occurs in 90 % of cases. It is commonly associated with adenocarcinoma.

Gynaecosmastia

It may occur occasionally. The histological types most frequently found are large cell and adenocarcinoma.

Dermatologic

Pigmentation, pruritus, lanugohirsuitism, acanthosis nigricans and erythema gyratum nigricans.

Vascular

Thrombophlebitis migrans, arterial thrombosis and non bacterial thrombotic endocarditis.

Hematologic

Anemia, hemolytic anemia, red cell aplasia, thrombocytopenic purpura, intravascular coagulopathy, hypofibrinogenemia and cosinophilia.

Immunologic

Dermatomyositis, systemic sclerosis, membranous glomerulo nephritis and rickets.

General systemic

Pyrexia, anorexia, cachexia and taste dysfunction.

Investigations

After a complete history and physical examination, imaging is the main first-line investigation:

- Chest X-ray is an important initial screen as it can reveal the following: the size and extent of any tumor, local spread, complications such as lymphadenopathy or pleural effusion, secondary lobar collapse, and hilar

or mediastinal lymph node enlargement. However, a 'normal' chest X-ray does not exclude primary lung malignancy

- Should be done in anteroposterior and lateral views using a high voltage (>125kV) to ensure adequate penetration through the tumor and the mediastinum
- Review of a prior X-ray is essential, if possible. The lesion may have been present for several years, and not changed in size, making the diagnosis less likely to be malignant
- If chest X-ray is 'normal' but suspicion for lung cancer exists, then a computed tomography (CT) scan should be done. (Note that chest X-ray is not considered adequate screening for a lung primary)

Blood tests should routinely be ordered as part of the work-up to evaluate the patient's overall fitness:

- Complete blood count (CBC) may reveal anemia or leukocytosis if there is secondary infection. Thrombocytosis or thrombocytopenia may be part of a paraneoplastic syndrome
- Liver function tests (LFTs) may be abnormal if there are metastases to the liver
- Renal function test should routinely be ordered as part of the work-up to evaluate the patient's overall fitness, and will influence the patient's ability to tolerate certain chemotherapeutic regimens

- Calcium group tests may reveal hypercalcemia secondary to either bone metastasis or a paraneoplastic process
- Cytology of sputum may reveal cancer cells; these are diagnostic if found, although negative cytology does not rule out primary lung malignancies

A specialist normally performs the following scans and biopsies:

- CT scan is necessary to evaluate primary disease and spread of suspected tumors locally and distantly and to assess lymph node involvement. CT is recommended as a staging procedure for patients with either non-small cell or small cell carcinoma
- Magnetic resonance imaging (MRI) has no advantage over CT scanning for evaluation of enlarged lymph nodes. MRI is not useful in routine staging, but can help to clarify the extent of tumor invasion in the mediastinum, root of neck, chest wall, and diaphragm if CT scanning results are equivocal
- Positron emission tomography (PET): accurate imaging investigation for possible intrathoracic lymph node involvement. It is best used in conjunction with CT scanning for accurate localization and interpretation. PET/CT is quickly gaining acceptance as the most informative test for ruling out more advanced disease in potentially resectable candidates. A negative PET and CT exam of the mediastinum may, at times, abrogate the need for surgical mediastinoscopic evaluation

- Enhanced MRI scans of the brain and isotope bone scans may detect asymptomatic occult metastases in many patients; therefore, brain imaging is mandatory for any patient being considered for surgical resection
- When CT scanning the thorax it seems sensible to include views of the liver and adrenal glands
- Biopsy by CT-guided needle, bronchoscopy, mediastinoscopy, or thoracoscopy: histologic confirmation of any suspicion of primary lung malignancies is essential to accurately diagnose the malignancy, ascertain its cell type and to plan the relevant treatment and predict the prognosis. Bronchoscopy is usually performed by a pulmonologist or thoracic surgeon, although some primary care physicians, especially in isolated areas, may offer this investigation. Transbronchial needle aspiration can be used to sample a parenchymal mass, mediastinal masses, or paratracheal lymph nodes
- Percutaneous needle biopsy: needle biopsy of a peripheral suspicious lesion, often under CT scanning guidance. It is useful for patients who are unfit for surgery. It has a high diagnostic success rate, but a negative biopsy should not necessarily exclude cancer
- Mediastinoscopy or mediastinotomy: an invasive procedure allowing endoscopic or direct views of the mediastinum. It is useful in evaluating the true extent of a mediastinal lymph node involvement. At the discretion of the surgeon, it might be omitted in a surgical candidate if there is no

evidence of mediastinal lymph node involvement by both PET and CT scanning, particularly if the tumor is peripheral, although a proportion of patients may have microscopic lymph node metastases

- Thoracoscopy and thoracentesis: an invasive endoscopic procedure allowing views of the pleura and pleural spaces, and aspiration of any pleural space fluid. It is useful in differentiating malignant pleural effusions from those secondary to consolidation distal to an obstruction lesion
- Biopsy of lymph nodes or pleura: surgical resection of axillary or cervical lymph nodes, or of the pleura, or percutaneous biopsies of them, may be needed in cases of diagnostic doubt or to assess local spread
- Cytology of sputum, bronchial washings, or pleural space fluid: cancer cells are diagnostic if found; but as this exam is highly insensitive, a negative cytology does not rule out primary lung malignancies

Staging

Staging is the process of finding out if cancer is localized or widespread. It will show if the cancer has spread to other body structures and, if so, how far. The treatment and prognosis (outlook for survival) for a patient with lung cancer depends, to a large extent, on the cancer's stage.

Staging of Small Cell Lung Cancer

For small cell lung cancers, a two-stage system is most often used. These are "limited stage" and "extensive stage". Limited stage usually means that the

cancer is only in one lung and in lymph nodes on the same side of the chest. Spread of the cancer to the other lung, to lymph nodes on the other side of the chest, or to distant organs indicates extensive disease. Many doctors consider small cell lung cancer that has spread to the fluid around the lung to be an extensive stage.

Small cell lung cancer is staged in this way because it helps separate tumors that can be treated more effectively with radiation therapy from those which cannot. About two-thirds of the people with small cell lung cancer will have extensive disease when their cancer is first found.

Staging of Non-Small Cell Lung Cancer (NSCLC)

The system most often used to describe the growth and spread of non-small cell lung cancer (NSCLC) is the TNM staging system, also known as the American Joint Committee on Cancer (AJCC) system. T stands for tumor (its size and how far it has spread within the lung and to nearby organs), N stands for spread to lymph nodes and M is for metastasis (spread to distant organs). In TNM staging, information about the tumor, lymph nodes, and metastasis is combined and a stage is assigned to specific TNM groupings. The grouped stages are described using Roman numerals from 0 to IV.

TNM STAGING OF LUNG CANCER

Supraclavicular	Scalene(ipsi-/contralateral)	Mediastinal (contralateral)	Mediastinal (ipsilateral)	Subcarinal	Hilar (contralateral)	Hilar (ipsilateral)	Peribronchial (ipsilateral)	LYMPH NODE (N)
+ /	+ /	+			/ +			N3
–	–	–	+ &/ +		–			N2
–	–	–	–	–	–	* + &/ +		N1
–	–	–	–	–	–	–	–	N0

Stage IV
M1 (any T, any N)

Stage III B

Stage III A

Stage II A **Stage II B**

Stage I A **Stage I B** **Stage II B**

M0

Stage 0
(Tis, N0, M0)

T1	T2	T3	T4	PRIMARY TUMOR (T)
a&b&c	any of a,b,c,d	(a&c)/b/d	(a&c)/d	Criteria
≤ 3 cm	> 3 cm	any	any	a. Size
No invasion proximal to the lobar bronchus	Main bronchus (≥ 2 cm distal to the carina)	Main bronchus (< 2 cm distal to the carina)	–	b. Endo-bronchial location
surrounded by lung or visceral pleura	Visceral pleura	Chest wall **/ diaphragm/ mediastinal pleura/ parietal pericardium	Mediastinum/ trachea/heart/ great vessels/ esophagus/ vertebral body/ carina	c. Local Invasion
–	Atelectasis/ obstructive pneumonitis that extends to the hilar region but doesn't involve the entire lung	Atelectasis/ obstructive pneumonitis of the entire lung	Malignant pleural/peri-cardial effusion or satellite tumor nodule(s) within the ipsilateral primary-tumor lobe of the lung	d. Other

METASTASES (M)

M0 : Abscent

M1 : Present

Separate metastatic tumor nodule(s) in the ipsilateral nonprimary-tumor lobe(s) of the lung also are classified M1

Tis : Carcinoma *in situ*

Staging is not relevant for Occult Carcinoma (Tx, N0, M0)

* Including direct extension to intrapulmonary nodes

** Including superior sulcus tumor

(& : and) (/ : or) (&/ : and /or)

MATERIALS AND METHODS

An open prospective study of female patients who attended Thoracic Medicine Department of Government General Hospital Chennai and Institute of Thoracic Medicine, Chetpet with Clinical and Radiological features suspicious of Primary Lung Cancer were studied over a period of 15 months between June 2006 and August 2007.

The study protocol included a detailed history regarding the onset and progress of the disease, lifetime exposure to smoking, detailed occupational history, residence and exposure to indoor air pollution due to burning of organic fuels. A detailed history regarding malignancy in the first degree relatives of patients was also taken. Female patients with a clinical assessment suggestive of primary lung cancer and proven histology only were included in this study. Total numbers of female Patients diagnosed to have Primary lung cancer were compared with the total numbers of male Patients with Primary Lung cancer diagnosed during the same period to detect the Sex ratio.

The complaints which were evaluated in detail included Cough, Sputum, hemoptysis, chest pain, dyspnoea, fever, weight loss, hoarseness of voice, dysphagia and symptoms suggestive of SVC obstruction, para neoplastic syndromes and systemic metastasis. A detailed general and systemic examination was performed.

All patients were subjected to baseline blood investigations, sputum for AFB smear and culture, sputum for non tuberculous culture, sputum for cytology, chest X-ray PA view and corresponding lateral view, ultrasound chest and abdomen. Computerized Tomography of the chest and upper abdomen was done to characterize the lesion further, to help to arrive at tissue diagnosis and to stage the disease. FOB was performed in all patients who were fit for the procedure. Computerized Tomography of brain and bone scan was done if indicated.

Following investigations helped in the histopathological confirmation of the diagnosis.

1. Computerized Tomography guided needle biopsy.
2. Ultrasound guided needle biopsy.
3. Endobronchial biopsy with fiber optic bronchoscopy.
4. Exision biopsy of accessible peripheral Lymph node.

Fiber optic bronchoscopy was performed with the single channel bronchoscope (Pentax, Japan). Under local anesthesia, 2 ml of 2 % lignocaine was injected transtracheally after test dose along with spraying of 4% lignocaine using hand atomizer just prior to the procedure. Lignocaine jelly was applied to the effective length of fiber optic bronchoscope. The fiber optic bronchoscope was passed transnasally/transorally in the supine position. The normal side was visualized first and then the suspected abnormal side. Biopsy was performed in

patients with obvious endo bronchial lesion. Mucosal brushings and washings were obtained from the area surrounding the abnormal segments on radiological basis in case of patients without endo bronchial lesion. A central tumor was defined as a tumor that was evident with in the bronchial tree at fiber optic bronchoscope and a peripheral tumor as one that was not visualized at bronchoscopy. X-ray wise, central tumor was defined as tumor arising at (or) close to the hilum, peripheral tumor as tumor arising beyond the hilum. Post broncoscopic sputum was sent for cytological examination. Patients were subjected to FNAC / Exision biopsy of peripheral Lymph node..

Computerized Tomography / Ultrasound guided needle biopsy was done in patients when indicated. The biopsy was done using Atovac Gun core biopsy needle. The needle size was 18G, 10 cm to 15 cm in length with 1 cm markings. The distal tip was ultrasound sensitive. The needle also has a over sheath cannula for Computerized Tomography guidance. The needle length was adjusted using pins. With computerized Tomography, Ultrasound guidance the lesion was localized, under cover of local anesthesia the needle length was adjusted according to the lesion and core biopsy obtained which was 2 cm to 2.5 cm bit.

The specimens obtained were:

Computerized Tomography guided needle biopsy

Fiber optic bronchoscope Brushing/Washing and biopsy

Ultrasound guided needle biopsy

Smears for cytology were fixed in isopropyl alcohol for 30 minutes and stained with Hematoxylin and eosin stain. Smears were air dried and fixed in methanol for 30 minutes. Air dried smears were fixed with MGG(Maygrunwald Giemsa) stain, slides were mounted and reported under microscope by cyto pathologist.

Biopsy specimens were fixed in formaldehyde (10%) for 24 hours. These slides were stained with Hematoxylin and eosin and reported by pathologist. Pleural fluid was centrifuged and smears stained in Hematoxylin and eosin.

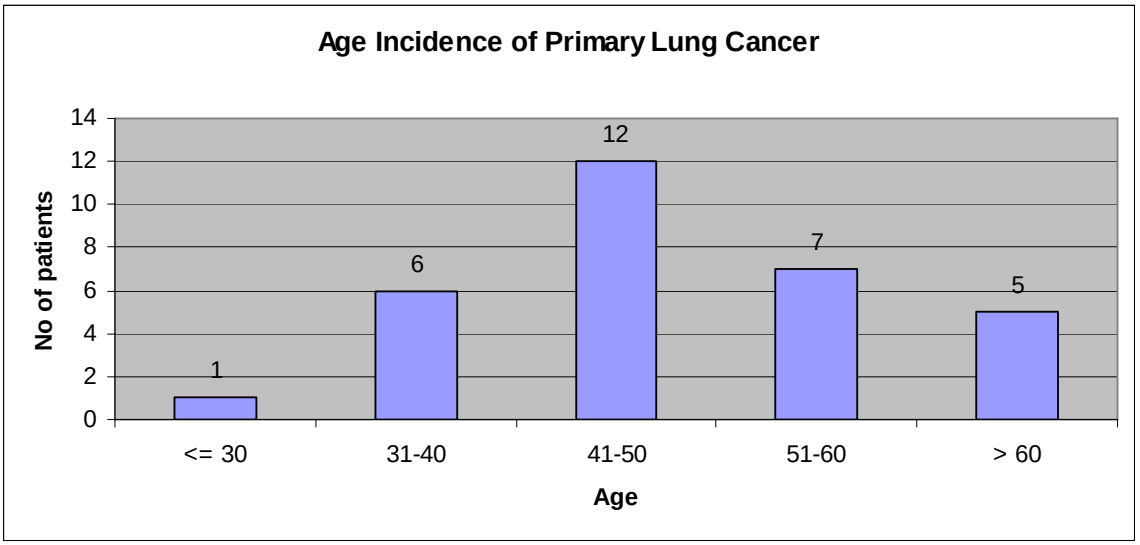
RESULTS

31 patients were included in the study. Pathological diagnosis was possible in 30 patients. Cell type diagnosis was not possible in one patient. However clinical and X-ray features suggestive of Primary Lung cancer and that was confirmed by presence of Malignant cells in pleural fluid and ultrasonography guided needle biopsy specimen.

Age:

In this study the age range was from 28 to 68 years.

Age Incidence of Primary Lung Cancer in this Study



Maximum number of patients presented between 41 to 50 years of age.

Sex Ratio:

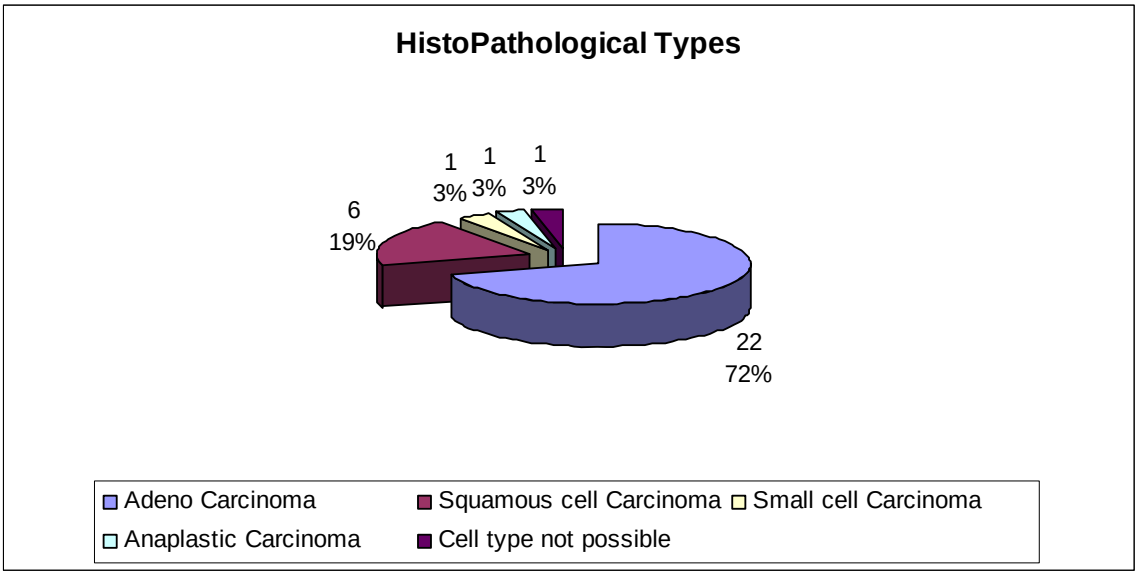
Total number of patients diagnosed to have Primary Lung Carcinoma during the period of study was 163(Male: 132 and Female: 31). Female (F: M ratio was 1:4.3) contribution was 19 % of the total.

Histo Pathological Types:

Out of 31 cases included in this study, 22 patients were Adeno Carcinoma, 6 patients were Squamous cell Carcinoma, 1 patient each for Small cell Carcinoma and Anaplastic Carcinoma.

Histo Pathological Types in this Study

Cell type	No of Patients	Percentage
Adeno Carcinoma	22	70.96
Squamous cell Carcinoma	6	19.35
Small cell Carcinoma	1	3.23
Ana plastic Carcinoma	1	3.23
Cell type not possible	1	3.23
Total	31	100.00



Risk Factors:

Smoking:

No Patient in this study was an active smoker. But exposure to ETS (Environmental tobacco smoke) was present in 14 patients (45.16 %). Out of 14 patients 9 patients (40.91 %) were Adeno Carcinoma, 3 patients (50 %) were Squamous Cell Carcinoma, ETS exposure was present in 1 patient each for Small cell and Anaplastic Carcinoma.

Indoor air pollution:

12 patients (38.71 %) gave definite History of exposure to biomass fuels like Cow dung cake and agricultural waste, wood and coal. Of these 12 patients, 10 (45.45 %) were Adeno Carcinoma.

Occupation:

Out of 31 patients, 1 patient (3.23 %) gave history of exposure to asbestos in the working place.

Radiation:

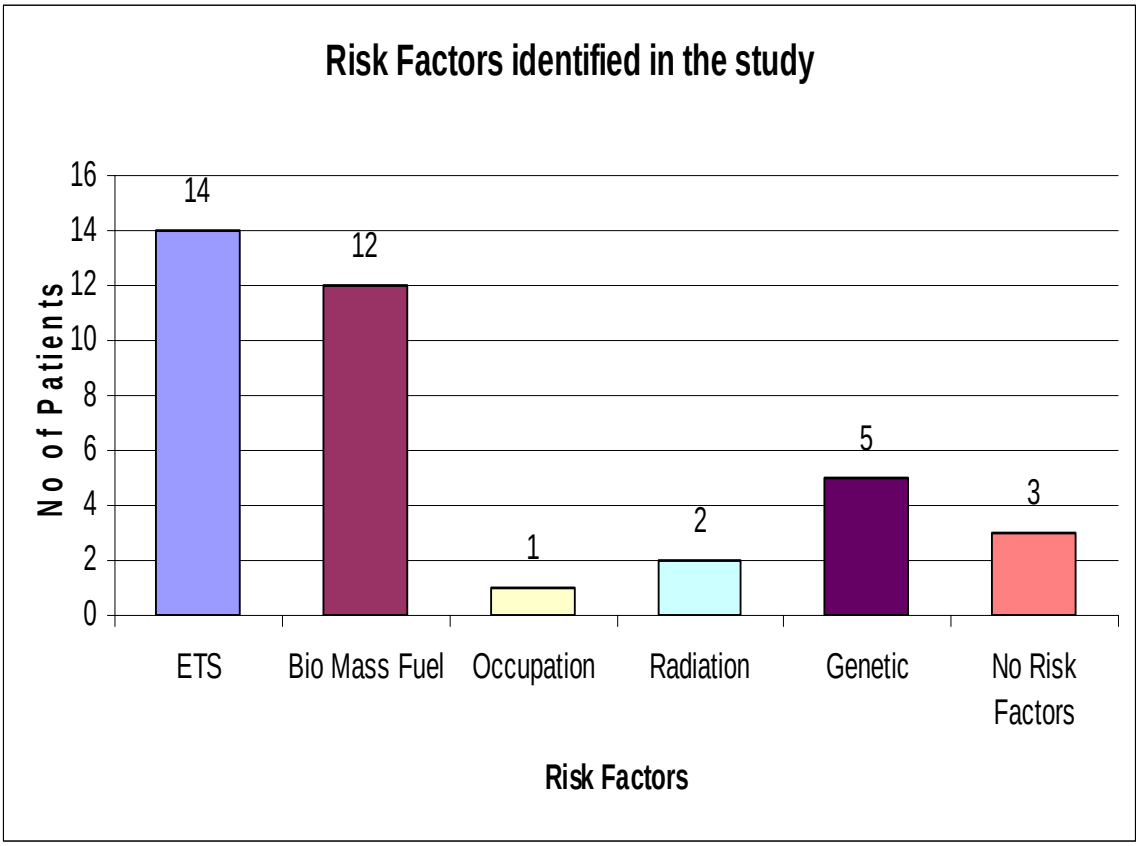
2 patients (6.45 %) gave history of exposure to radiation. Both were Adeno Carcinoma (9.09 %).

Genetic Factors:

Genetic predisposition for Malignancy was present in 5 patients (16.13 %) in this study. Out of which 4 patients (18.18 %) were Adeno Carcinoma. Out of 4 patients 2 patients gave history of previous Malignancy like Hodgkin's lymphoma and Carcinoma cervix (Squamous cell). Other 2 patients (9.09 %) had family history of Malignancy in breast and Lung.

Possible Risk Factors identified in this study

CELL TYPE	RISK FACTORS									
	ENVIRONMENT								GENETIC	
	ETS		Bio-Mass Fuels		Occupation		Radiation			
	No.	%	No.	%	No.	%	No.	%	No.	%
Adeno Carcinoma	9	40.91	10	45.45	1	4.55	2	9.09	4	18.18
Squamous Cell Carcinoma	3	50	1	16.67	0	0	0	0	1	16.67
Small Cell Carcinoma	1	100	0	0	0	0	0	0	0	0
Ana plastic Carcinoma	1	100	1	100	0	0	0	0	0	0
Total	14	45.16	12	38.71	1	3.23	2	6.45	5	16.13



- One patient whose cell type not possible included.
- No Patient in this study gave history of Exposure to Environmental Industrial pollutants.
- Prior history of ATT present in only one case C.No 24

Clinical Features:

The most common pulmonary symptoms were breathlessness, cough, chest pain and hemoptysis. Of this breathlessness was present in 16 patients (51.61 %), cough was present in 13 patients (41.94 %) followed by chest pain in 13 patients (41.94 %) and hemoptysis in 10 patients (32.26 %).

Salient Features of different Cell Types

SYMPTOM	CELL TYPE									
	Adeno		Squamous		Small cell		Anaplastic		Total	
	No	%	No	%	No	%	No	%	No	%
Cough	8	36.36	4	66.67	1	100	0	0	13	41.94
Chest Pain	11	50	1	16.67	0	0	1	100	13	41.94
Hemoptysis	4	18.18	5	83.33	1	100	0	0	10	32.26
Breathlessness	11	50	3	50	1	100	1	100	16	51.61

- One patient whose cell type diagnosis was not possible had cough and breathlessness.
- Out of 3 patients with Bronchioloalveolar subtype of Adeno Carcinoma, 2 patients presented with bronchorrhea.

SVC obstruction was present in 2 patients (6.45 %) and the cell type was squamous cell Carcinoma (i.e. SVC obstruction was present in 33.33 % of patients with squamous cell carcinoma). CNS metastasis was seen in 3 patients (9.68 %), of which 1 patient was small cell carcinoma (100 %), 1 patient was squamous cell carcinoma (16.67 %) and 1 patient was adeno carcinoma (4.55 %). Liver metastasis was seen in 1 patient (3.23 %) that was adeno carcinoma (4.55 %). Bone (Ribs & Vertebral) metastasis was seen in 3 patients (9.68 %) of which 2 patients were adeno carcinoma (9.09 %) and 1 patient was anaplastic carcinoma (100 %). Hoarseness of voice was present in 4 patients (12.90 %) and actual vocal cord palsy was seen in 3 patients.

Chest X-ray Features:

The most common presentation was mass lesion 54.84 % (n=17) followed by pleural effusion 35.48 % (n=11).

Radiologic Manifestations of different Cell Types

FINDINGS	CELL TYPE									
	Adeno		Squamous		Small cell		Anaplastic		Total	
	No	%	No	%	No	%	No	%	No	%
* Lt Side	10	45.45	4	66.67	0	0	0	0	14	45.16
Rt Side	8	36.36	2	33.33	1	100	0	0	11	35.48
Bi lateral	4	18.18	0	0	0	0	1	100	5	16.13
Pulmonary mass	15	68.18	1	16.67	0	0	1	100	17	54.84
Hilar mass	3	13.64	4	66.67	1	100	0	0	8	25.81
Mediastinal mass	1	4.55	0	0	0	0	0	0	1	3.23
Cavity	0	0	1	16.67	0	0	0	0	1	3.23
Consolidation	2	9.09	0	0	0	0	0	0	2	6.45
Collapse	2	9.09	3	50	1	100	0	0	6	19.35
#Pleural Effusion	8	36.36	2	33.33	1	100	0	0	11	35.48
Coin Shadow	0	0	0	0	0	0	0	0	0	0
Rib/Vertebral erosion	2	9.09	0	0	0	0	0	0	2	6.45
Diaphragm Palsy	1	4.55	0	0	0	0	0	0	1	3.23

* 1 patient who was not typed had Lt Side involvement

\# 1 patient not typed

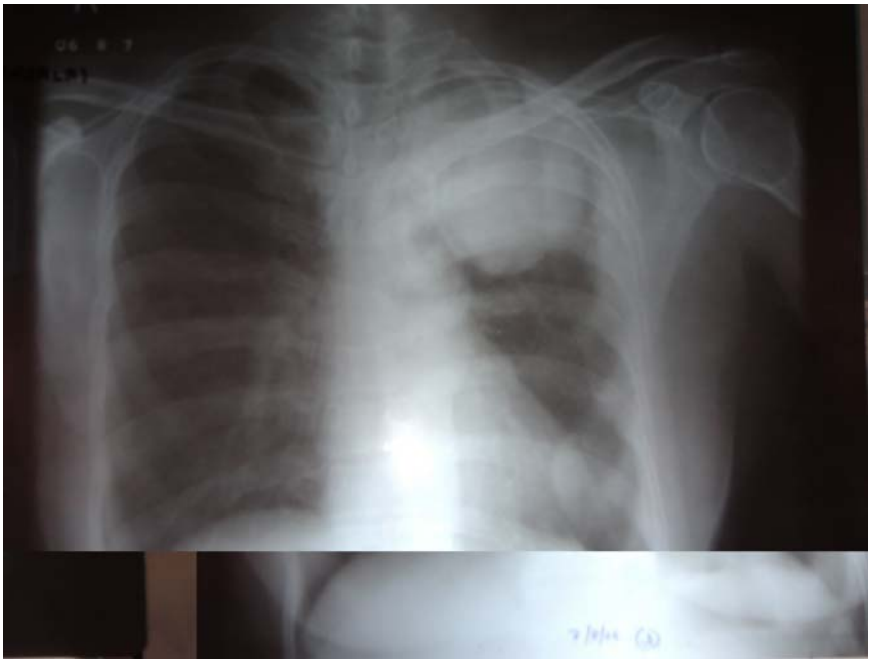


Fig. 1 - Chest Skiagram PA view – showing mass (Left) upper zone.

Fig. 2 – Computerized Tomography scan – showing mass (Left) upper lobe posterior segment of the above patient.

Fig.3 Chest Skiagram PA view – showing (left) hilar prominence

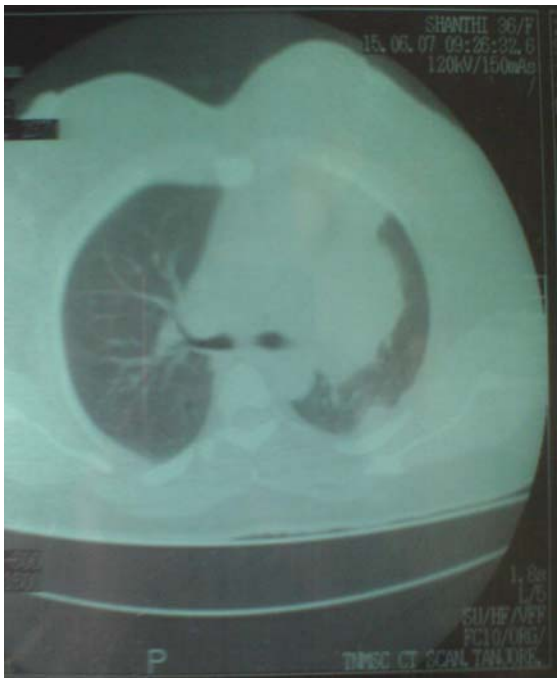


Fig.4 Computerized Tomography scan – showing (left) hilar mass lesion of the above patient

Diagnostic Modalities:

Computerized Tomography scan was done in all 31 patients. Computerized Tomography helped in histo pathological diagnosis by way of computerized Tomography guided needle biopsy of suspected mass in 12 patients (38.71 %). Bronchus cut off sign was positive in 3 patients. Computerized Tomography diagnosed 4 patients with mediastinal nodes, 2 patients with rib/vertebral metastasis and 2 patients with nodules in the lung which were not seen on the chest X-ray.

Fiber optic bronchoscope was done in 26 patients (83.87 %). Bronchial brushing cytology yield was 26.92 %(n=7). Endobronchial biopsy yield was 15.38% (n=4).

Ultrasonography of the chest was useful in identifying peripheral tumors close to the chest wall. It helped in the histo pathological diagnosis by the way of guided needle biopsy of suspected mass in 8 patients (25.81 %).

Supra clavicular Node FNAC/Biopsy yielded positive results in 6 patients (19.35 %).

Primary diagnostic modalities for Histopathological documentation

Cell Type	Total Number of Cases	Methods					
		CT		FOB		USG	
		NO	%	NO	%	No	%
Adeno	22	10	45.45	5	22.73	7	31.82
Squamous	6	1	16.67	5	83.33	0	0
Small Cell	1	0	0	1	100	0	0
Anaplastic	1	1	100	0	0	0	0
Not typed	1	0	0	0	0	1	100
Total	31	12	38.71	11	35.48	8	25.81

Staging:

Staging was done based on clinical, radiographic and bronchoscopic findings. Patients in whom bronchoscopy was not done due to poor performance status, staging was done by means of other two methods.

Non small cell carcinoma patients were staged based on TNM classification whereas small cell carcinoma patient was staged in a simple fashion in to two categories like limited disease and extensive disease.

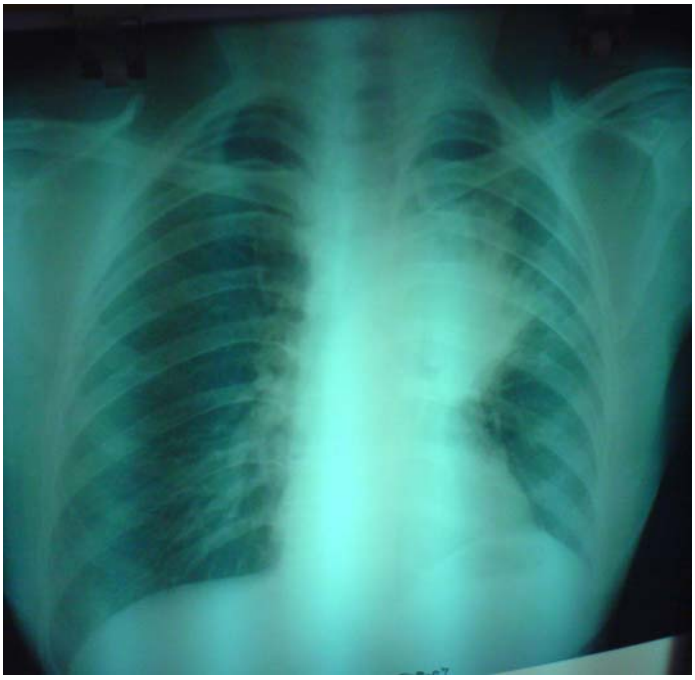
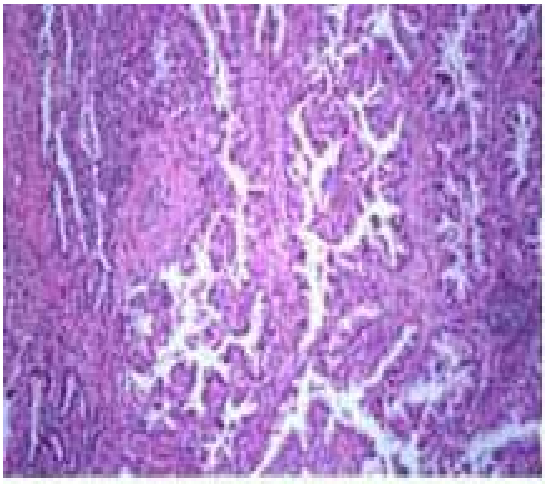
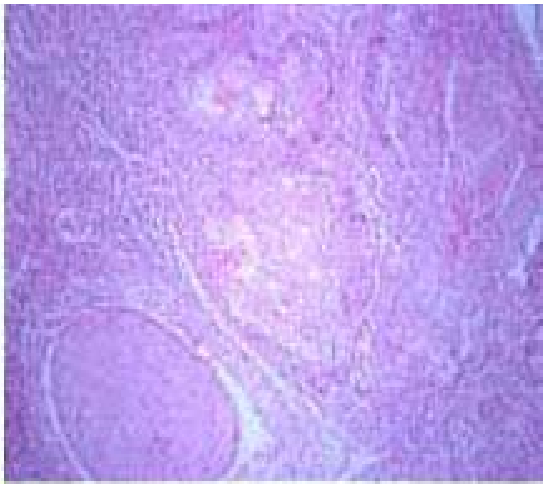


Fig.5 Chest Skiagram PA view – showing (left) hilar mass lesion with elevation of (left) hemidiaphragm



Lung cancer histology.
Adenocarcinoma-characterized by heterogeneous differentiation in the same tumor.

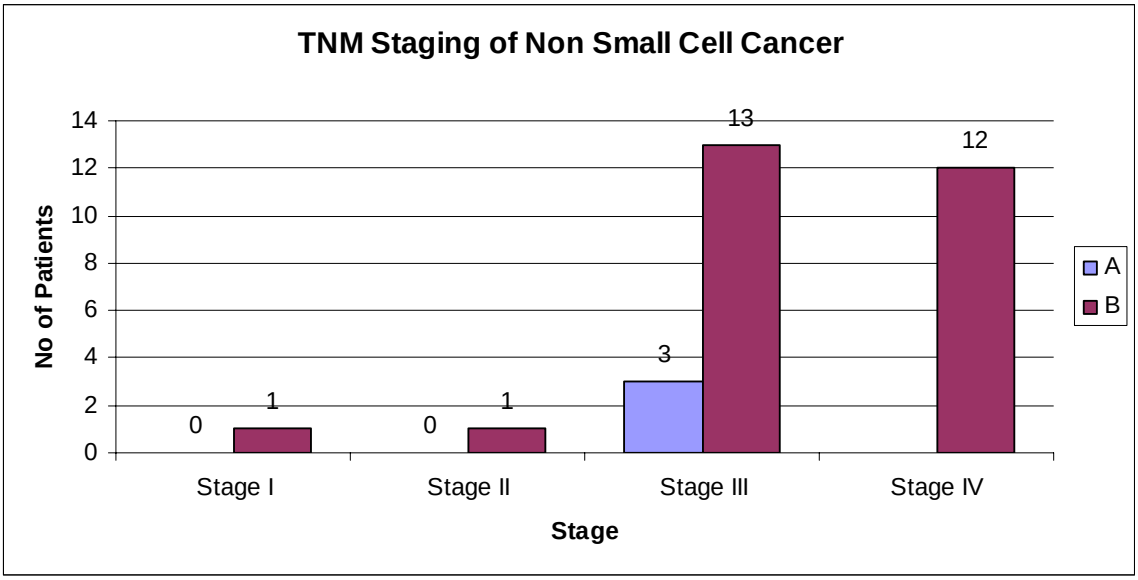


Lung cancer histology
Squamous cell-characterized by the presence of cytokeratin differentiation with keratinization and intercellular bridges.

Fig. 6

TNM Staging of Non small cell lung cancer in this study

Cell Type	Stage I		Stage II		Stage III		Stage IV
	A	B	A	B	A	B	
Adeno	-	-	-	1	3	10	8
Squamous	-	1	-	-	-	3	2
Anaplastic	-	-	-	-	-	-	1
Not possible	-	-	-	-	-	-	1
Total	-	1	-	1	3	13	12
Percentage	0	3.33	0	3.33	10	43.33	40



- 1 patient who was not typed included
- 1 patient with small cell carcinoma had extensive disease
- Most of the patients were in stage III B (43.33 %) and IV (40 %) at the time of presentation (n=25).

DISCUSSION

Lung Cancer is one of the commonest malignant neoplasm in India both in males and females, and the Gender difference is narrowing. Complex circumstances like genetic predisposition, environmental exposure, life style habits combine over a lifetime to initiate and promote tumor growth in the lung.

In this prospective study of 31 patients, 30 patients had confirmed pathological diagnosis, but in 1 patient malignant cell could be identified but cell type was not possible.

The age range was from 28 to 68 years. Maximum number of patients in this study was between 41 and 50 years. Mean age was 49 years. This is less than the study conducted by Jindal SK and Behera D 1990(5) where the mean age was 52 years.

The female contribution to Primary lung malignancy was 19% in this study. In the previous study conducted in our institution by Rajashekaran et al in 1993, the female contribution was 3% (27). In another study conducted during 2000 in our institution, the female contribution was 14%. This shows a definite trend towards increasing incidence in females.

The most common histopathological type in this study was Adeno Carcinoma (70.96 %). The second most common type was Squamous cell Carcinoma (19.35 %). This is in corroboration with the study done by T.Behera,T.Balamugesh 2005 (12).

Tobacco smoking is the most important risk factor for lung cancer. None of the patients in this study was a smoker. But exposure to Environmental tobacco smoke was present in 45 % of patients.

Environmental tobacco smoke (ETS) is an important indoor as well as outdoor air pollutant that may be a contributing risk factor. Exposure to environmental tobacco smoke was present in 14 patients (45.16 %). This is less compared to the study done by T.Behera , T. Balamugesh, 2005 (12), where the exposure was 53 %. Adeno and Squamous cell carcinoma were almost equally distributed in patients exposed to ETS in this study. ETS exposure was present in one patient with small cell carcinoma.

Significant exposure to domestic biomass cooking fuels like wood, cowdung cake, agricultural waste, coal etc was present in 12 patients (38.71 %). This is less compared to the study done by T.Behera, T.Balamurugesh, 2005 (12). Among 12 patients 10 were Adeno Carcinoma.

Exposure to occupational carcinogens like asbestos was present in 1 patient (3.23 %) and the cell type was Adeno Carcinoma. In the study conducted by DC Vos Irvine and colleagues, the incidence was 5.7 % (8).

Exposure to Radiation was present in 2 patients (6.45 %). Of these 2 patients, one patient gave history of Radiotherapy treatment for Hodgkin's Lymphoma 15 years back and another patient is residing in area of atomic power station for more than 25 years. Genetic Predisposition to get cancer was present in 5 patients (16.13 %).

Most common pulmonary symptom in this study was breathlessness 16 patients (51.61 %) followed by Cough 13 patients (41.94 %) and chest pain 13 patients (41.94 %). Cough and Hemoptysis were present predominantly in patients with Squamous cell carcinoma. Increased breathlessness in this study could be attributed to the Later stage of the disease in most of the patients and to the pleural involvement.

The most common radiological presentation was mass lesion, which was seen in 17 patients (54.84 %) followed by pleural effusion in 11 patients (35.48 %). Adeno Carcinoma present as a peripheral mass is 68 % and as a central lesion in 13 % of patients. Squamous cell carcinoma present as a peripheral mass in 16 % and as a central lesion in 66 % of patients. 1 patient of small cell carcinoma was present as a central lesion (100 %). This is in corroboration with

the study done by D.Behera, T.Balamugesh 2004 (45). 2 Patients with bronchiloalveolar sub type of Adeno Carcinoma presented as consolidation in X-ray.

Post bronchoscopic sputum cytology was positive in 2 patients (6.45 %) and the most common tumor associated was squamous cell carcinoma.

Computerized Tomography study was done in all 31 patients. Computerized Tomography guided needle biopsy of suspected mass was done in 14 patients. Positive results were obtained in 12 patients (85.71 %).

USG guided needle biopsy of suspected mass lesion was positive in all patients who underwent the procedure (100 %). CT/USG guided needle biopsy helped in the diagnosis of 20 patients (65 %) out of 31 patients. Whereas in the study conducted by C R PAYNE et al (46), the yield was much higher (88 %).

Fibre optic bronchoscopy was done in 26 patients (83.87 %). It helped in diagnosis by the way of endo bronchial Biopsy in 4 patients (15.38 %) and by bronchial brushing cytology in 7 patients (26.92 %).This is in corroboration with the study conducted by Gupta PK et al Rajasthan, in 1993 (50) where the combined yield of bronchial biopsy and brush cytology was 45 %.

Supraclavicular Lymph node FNAC/biopsy yielded positive results in 6 patients (19.35 %) whereas in the study conducted by Jindal SK and Behera D (5), the yield was 10.7 %.

In this study majority of the patients (83.33 %) were in the advanced stages of the disease (IIIB and IV) at the time of presentation. In the study conducted by Rajendra Prasad et al 2004 (49), 74.2 % of patients were in the advanced stage. In the study conducted by Rajashekaran et al 1993 (27), 96 % were in the advanced stage of the disease.

CONCLUSIONS

- There is definitely a increasing trend in the incidence of Primary Lung Cancer in females when compared with the previous studies conducted in our institution. This disturbing trend inline with global situation needs further evaluation.
- Maximum number of patients was between 41-50 years of age.
- Environmental Tobacco Smoke and Bio-mass cooking fuel exposure constituted about 84 % of Risk Factors identified in this study.
- In addition to the above risk factors, occupational pollutants / Radiation have an additive effect in the background of Genetic predisposition in the causation of Lung Cancer in females.
- Most common Pathological cell type in females was Adeno Carcinoma.
- Most common Radiological presentation was Mass lesion followed by pleural effusion.
- 83 % of patients were in the advanced stage of disease at the time of presentation.

- Fibreoptic bronchoscope Biopsy and Brushing / Computerized Tomography / Ultrasound guided core needle Biopsy were valuable tools to get a tissue diagnosis.
- Lung lesions in females in high risk age group of 40 years and above should be investigated without gender bias thoroughly to rule out malignancy. This approach may result in diagnosing malignancy at an early stage. Primary Lung malignancies are common only in smokers, is proved as a misconception as evidenced by this study.

Short Comings of this Study

- The number of cases studied was only 31.
- Bronchoscopy not done in 5 patients due to poor performance status.
- 3 patients didn’t reveal any risk factors.
- Exact quantification of exposure to risk factors not possible.

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ABBREVIATION

DRC	-	DNA Repair Capacity
ETS	-	Environmental Tobacco Smoke
NSCLC	-	Non Small Cell Lung Cancer
SCLC	-	Small Cell Lung Cancer
ACTH	-	Adreno Corticotropic Hormone
GHRH	-	Growth Hormone Releasing Hormone
SVC	-	Superior Venacava
FOB	-	Fibreoptic Bronchoscope
FNAC	-	Fine Needle Aspiration Cytology
ATT	-	Anti Tuberculous Treatment
CNS	-	Central Nervous System

MASTER CHART

S.No	Age (Years)	Cell Type	Risk Factors	Pulmonary Symptoms	Chest X-ray	Diagnostic Mode	Staging
1	65	2	1	1,2,3,4	2,5,9	3	7
2	60	2	5	3,4	1,9	3	6
3	40	1	1	3,4	2,5,8,9	3	7
4	51	1	4,5	2,4	2,4	1	6
5	51	1	2	2,4	2,5,9	2	6
6	50	1	2	4	1,4	1	4
7	37	1	1,3	0	1,13	1	7
8	50	3	1	1,3,4	2,5,8,9	3	9
9	60	2	1	1,4	1,4,5,8	3	6
10	42	1	1	0	1,4,11	1	6
11	55	1	5	2,4	1,4,8,12	1	5
12	65	1	1	1,2	1,4,5	1	6
13	47	1	2	1	2,7	1	5
14	65	1	5	3	3,4	1	7
15	45	0	0	1,4	1,9	2	7
16	40	1	2	1	2,4	2	6
17	50	1	1	2	1,4,9	1	6
18	50	4	1,2	2,4	3,4	1	7
19	41	1	1,2	1,3,4	3,4	2	7
20	45	1	2	2	1,4,9	2	7
21	40	1	4	2,4	1,4	3	6
22	55	1	1,2	1,4	2,9	3	6
23	45	2	0	1,3	1,5,8	3	7
24	32	1	2	1,2,4	3,4	2	7
25	28	2	0	3	2,6	3	2
26	68	1	1	1,2,3	1,4,9	3	6
27	39	1	5	2	1,4	3	7
28	45	1	1	4	2,9	1	6
29	49	1	2	1	2,7	2	5
30	57	1	2	2,4	3,4,11	2	7
31	63	2	1,2	1,3	1,5,8	1	6

KEY TO MASTER CHART

Cell type		**Risk Factors**		**Pulmonary Symptoms**	
Not possible	0	No Risk Factors	0	Nil	0
Adeno Carcinoma	1	ETS	1	Cough	1
Squamous Cell CA	2	Bio Mass Fuels	2	Chest Pain	2
Small Cell Carcinoma	3	Occupation	3	Hemoptysis	3
Anaplastic Carcinoma	4	Radiation	4	Breathlessness	4
		Genetic	5		
		Active Smoking	6		
Chest X-ray		**Diagnostic mode**		**Staging**	
Lt Side	1	CT guided Biopsy	1	**NSCLC**	
Rt Side	2	USG guided Biopsy	2	IA	1
Bilateral	3	Fiber optic		IB	2
Pulmonary Mass	4	Bronchoscope	3	IIA	3
Hilar Mass	5			IIB	4
Cavity	6			IIIA	5
Consolidation	7			IIIB	6
Collapse	8			IV	7
Pleural Effusion	9				
Coin Shadow	10			**SCLC**	
Rib/Vertebral Erosion	11			Limited Disease	8
Diaphragm Palsy	12			Extensive Disease	9
Mediastinal Mass	13				